REMARKS

Applicants respectfully request entry of the foregoing and reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks that follow.

Claims 1, 3-10 and 12-37 are pending in the application, new claims 22-37 having been added above.

By the above amendments, claims 1 and 19-21 are amended by replacing "prevent" with --eliminate-- to address the §112, first paragraph, issue. Support for this amendment can be found at least at page 14, paragraph 57 of the specification. Additionally, claims 1, 10 and 21 are amended by deleting the word "retinoids." Also, claim 10 and 12 are amended to address the §112, second paragraph, issue by deleting the words "being capable of." Claims 8 and 17 are amended to address the §112, second paragraph, issue by providing more conventional Markush Group language. Finally, new claims 22-37 are added to further define exemplary embodiment of the invention. Support for new claims 22-37 can be found at least at original claims 2-9.

Applicants thank the Examiner for the courtesies extended to their representatives, Mary Katherine Baumeister and Martin A. Bruehs, during the personal interview of February 21, 2003. In this regard, the Examiner's Interview Summary provides a fair assessment of the issues discussed during the interview.

Applicants also thank the Examiner for withdrawing the double patenting rejection over U.S. Patent No. 6,060,061 and U.S. Patent No. 5,658,581 in view of the terminal disclaimer of the '061 patent and the remarks presented in the Amendment filed on October

15, 2002, which pointed out that a terminal disclaimer was not required to obviate the rejection over the '581 patent.

Furthermore, Applicants thank the Examiner for acknowledging that claims 19-20 would be allowable if amended to address the §112, first paragraph issue. In view of the above amendments, Applicants submit that claims 19-20 are in condition for allowance.

Turning now to the Official Action, claims 1-21 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which is not adequately described in the specification. In order to obviate this rejection, Applicants have amended claims 1 and 19-21. In particular, Applicants have amended these claims by replacing the word "prevent" with the word --eliminate--. Support for this amendment can be found at least at page 14, paragraph 57 of the specification.

Applicants respectfully request reconsideration and withdrawal of the §112, first paragraph, rejection.

Claims 8-10 and 12-18 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. For at least the reasons that follow, withdrawal of the rejection is in order.

First, Applicants have amended claims 10 and 12 to address the rejection of these claims for use of the words "capable of." Specifically, Applicants deleted the words "being capable of" from claims 10 and 12 to obviate the rejection.

Additionally, with respect to the rejection of claims 8 and 17 for use of improper Markush Group language, Applicants have amended these claims to obviate the rejection.

That is, Applicants have amended claims 8 and 17 to include more convention Markush Group language.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the §112, second paragraph, rejections.

Claims 1, 3-10, 12-18 and 21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Parker (U.S. Patent No. 5,039,695) in view of Farng (U.S. Patent No. 5,643,584). For at least the reasons that follow, withdrawal of the rejection is in order.

The present invention relates to the use of a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist in a cosmetic, pharmaceutical or dermatological composition for topical application, intended, in particular, for the treatment of sensitive skins, as well as to a composition containing a histamine antagonist, an interleukin-1 antagonist and/or a TNF-alpha antagonist for the purpose of decreasing or even abolishing the irritant effects of certain products, and in particular of certain active agents used in the cosmetics, pharmaceutical or dermatological field. See specification at page 1, paragraph 2.

Parker relates to certain aryl and heteroaryl-alkyl-pyrrole carboxylic acid components of Formula I. Parker is also directed to the pharmacological use of the compounds of Formula I as interleukin-1 inhibitors effective in alleviating interleukin-1 mediated conditions. See Parker at column 1, line 55 to column 2, line 9.

Parker does not disclose or fairly suggest each feature of the presently claimed invention. For example, Parker discloses a composition comprising an IL-1 antagonist for use as a mediator in treating psoriasis. Nowhere, however, does Parker disclose or fairly

suggest a composition comprising an amount of at least one agent sufficient to elicit an irritant side-effect when used in a composition that does not include an IL-1 antagonist or a TNF-alpha antagonist, wherein the irritant agent is an active agent in the composition and an amount of at least one compound selected from the group consisting of an IL-1 antagonist, TNF-alpha antagonist or combination thereof sufficient to eliminate, alleviate or antagonize the irritant side effect elicited by the active agent, as defined in independent claims 1 and 10. In fact, the Official Action itself admits at page 6 that Parker "lacks an agent which produces an irritant." Thus, Parker fails to disclose or fairly suggest any agent sufficient to elicit an irritant side effect, let alone an agent selected from the group consisting of alpha-keto acids, beta-keto acids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, andimetabolites, vitamin D, and depigmentation agents, as defined in independent claims 1, 10 and 21.

Farng fails to overcome the above deficiencies of Parker. That is, Farng relates to aqueous gel vehicles for retinoids. More specifically, Farng relates to micronized particles of retinoids, particularly tretinoin, incorporated into aqueous gel vehicles to provide a gel composition for topical application of such retinoids to the skin. See Farng at column 1, lines 8-12.

Because Farng only discloses using retinoids, and because independent claims 1, 10 and 21, as amended above, define the at least one agent sufficient to elicit an irritant side effect as being selected from the group consisting of alpha-keto acids, beta-keto acids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D, and depigmentation agents, Applicants submit that Farng fails to overcome the above

deficiencies of Parker. That is, the combination of Parker and Farng would not have rendered obvious the compositions defined in independent claims 1, 10 and 21 because Farng fails to disclose or fairly suggest using an amount of at least one agent sufficient to elicit an irritant side effect, as defined in these claims, in combination with at least one compound selected from the group consisting of IL-1 antagonists, TNF-alpha antagonists and combinations thereof sufficient to eliminate or alleviate the irritant side effect elicited by the irritant agent.

For at least these reasons, claims 1, 10 and 21, and the claims depending therefrom, would not have been obvious over Parker in view of Farng. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

With respect to the response to Applicants' arguments provided at page 6 of the Official Action, Applicants provide the following remarks.

The Official Action at page 6 indicates that the argument that the present invention relates to the use of histamine antagonists as well as IL-1 antagonists and/or TNF-alpha antagonists is not persuasive because it is not within scope with the independent claims. Applicants submit that this argument is, however, relevant to patentability of dependent claims 3-4 and 12-13, which further define the composition of independent claims 1 and 10 as comprising at least one histamine antagonist. That is, claims 3-4 and 12-13 are further distinguished from the cited prior art because the cited prior art fails to disclose or fairly suggest a composition comprising an amount of at least one agent sufficient to elicit an irritant side effect, at least one compound selected from the group consisting of IL-1

antagonist, TNF-alpha antagonist and combinations thereof and further comprising at least one histamine antagonist.

For at least these reasons, dependent claims 3-4 and 12-13 also would not have been obvious over the combination of Parker in view of Farng.

From the foregoing, Applicants earnestly solicit further and favorable action in the form of a Notice of Allowance.

If there are any questions concerning this paper or the application in general, Applicants invite the Examiner to telephone the undersigned at the Examiner's earliest convenience.

Respectfully submitted,

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Mark-up of Claims 1, 8, 10, 12, 17, and 19-21

1. (Twice Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

-- an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition,

-- an amount of at least one compound selected from the group consisting of interleukin-1 antagonists, TNF-alpha antagonists and combinations thereof, sufficient to [prevent] eliminate or alleviate said irritant side-effect, and a cosmetically, dermatologically or pharmaceutically acceptable medium therefor, wherein the agent which produces the irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, [retinoids,] anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D and depigmentation agents.

8. (Amended) The composition of Claim 1, further comprising at least one active agent selected from the group consisting of an anti-bacterial, an antiparasitic agent, an antifungal agent, an anti-inflammatory agent, an antipruriginous agent, an anesthetic agent, an antiviral agent, a keratolytic agent, a free-radical scavenging agent, an antiseborrheic agent, an antidandruff agent [and] , an anti-acne agent, [agents and/or

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agents] an agent which [modulate the] modulates differentiation of skin, an agent which modulates [and/or the] proliferation [and/or the] of skin and an agent which modulates pigmentation of skin.

10. (Twice Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising

an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

at least one compound selected from the group consisting of interleukin-1 antagonists, TNF alpha antagonists and combinations thereof, in an amount effective to antagonize said irritant side-effect;

and a cosmetically, dermatologically or pharmaceutically acceptable medium therefor, said compound [being capable of] inhibiting the IL-1-induced adhesion of macrophages to endothelial cells, inhibiting the IL-1-induced release of superoxide anions from neutrophils, inhibiting the TNF alpha-induced adhesion of macrophages to endothelial cells, inhibiting the TNF alpha-induced release of superoxide anions from neutrophils, inhibiting the mitogenic activity of TNF alpha by dermal fiproblasts, or inhibiting the release of interleukin-1 or TNF alpha by phorbol ester induced differentiated monocytes, and wherein the agent which produces an irritant side-effect is selected from the group

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consisting of alpha-keto acids, beta-keto acids, [retinoids,] anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D, and depigmentation agents.

12. (Amended) The composition of Claim 10, further comprising at least one histamine antagonist, said histamine antagonist [being capable of] inhibiting the contraction of smooth muscles induced by the administration of histamine or inhibiting the release of histamine by stimulated mast cells.

17. (Amended) The composition of Claim 10, further comprising at least one active agent selected from the group consisting of an anti-bacterial agent, an antiparasitic agent, an antifungal agent, an anti-inflammatory agent, an antipruriginous agent, an anesthetic agent, an antiviral agent, a keratolytic agent, a free-radical scavenging agent, a antiseborrheic agent, an antidandruff agent [and] , an anti-acne agent, an agent [agents and/or agents] which [modulate the] modulates differentiation of skin, an agent which modulates [and/or the] proliferation of skin, and an agent which modulates [and/or the] pigmentation of skin.

19. (Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

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an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

an amount of at least one TNF-alpha antagonist sufficient to [prevent] eliminate or alleviate said irritant side-effect; and

a cosmetically, dermatologically or pharmaceutically acceptable medium therefor wherein the agent which provides the irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D and depigmentation agents.

20. (Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

an amount of at least one interleukin-1 antagonist and at least one TNF-alpha antagonist, sufficient to [prevent] eliminate or alleviate said irritant side-effect; and

a cosmetically, dermatologically or pharmaceutically acceptable medium therefor.

21. (Amended) A composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

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an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist, and wherein said irritant agent is an active agent in said composition;

an amount of at least one interleukin-1 antagonist, sufficient to [prevent] eliminate or alleviate said irritant side-effect; and

a cosmetically, dermatologically or pharmaceutically acceptable medium therefor, said agent being selected from the group consisting of alpha-keto acids, beta-keto acids, [retinoids,] anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D and depigmentation agents.